EXHIBIT C

AHFS DRUG INFORMATION 2005

American Society of Health-System Pharmacists®

Printed in the United States of America.

LIBRARY OF CONGRESS CATALOG CARD NUMBER: 59-7620

INTERNATIONAL STANDARD BOOK NUMBER (ISBN): 1-58528-039-9

INTERNATIONAL STANDARD SERIAL NUMBER (ISSN): 8756-6028

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Lotion	0.05%	DesOwen® (with emollient and propylene glycol), Galderma
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*available by nonproprietary name

Desoximetasone

Desoxymetasone

■ Desoximetasone is a synthetic fluorinated corticosteroid.

Uses

Desoximetasone shares the actions of the other topical corticosteroids and is used for the relief of the inflammatory manifestations of corticosteroid-responsive dermatoses.

Dosage and Administration

Topical desoximetasone is applied sparingly in a thin film and rubbed gently into the affected area twice daily.

Chemistry and Stability

■ Chemistry

Desoximetasone is a synthetic fluorinated corticosteroid. The drug occurs as a white crystalline powder and is very slightly soluble in water and soluble in alcohol.

■ Stability

Desoximetasone preparations should be stored in well-closed containers at 15–30°C.

For further information on chemistry, pharmacology, absorption, uses, cautions, methods of application, and use of occlusive dressings in therapy with desoximetasone, see the Topical Corticosteroids General Statement 84:06.

Preparations

Desoximetasone

Topical		
Cream	0.05%	Desoximetasone Cream, Major, Taro, Zenith Goldline
		Topicort® LP, Medicis
	0.25%*	Topicort®, Medicis
Gel	0.05%	Desoximetasone Gel, Taro
		Topicort® (with SD alcohol 40 20% w/w), Medicis
Ointment	0.25%	Topicort® (with propylene glycol), Medicis
		Desoximetasone Ointment, Fougera, Taro

*available by nonproprietary name

Diflorasone Diacetate

■ Diflorasone diacetate is a synthetic fluorinated corticosteroid.

Uses

Diflorasone diacetate shares the actions of the other topical corticosteroids and is used for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

Dosage and Administration

Topical diflorasone diacetate cream is applied sparingly in a thin film and rubbed gently into the affected area 2–4 times daily; the emollient cream preparation (Florone E®) and the ointments, including the enhanced-potency preparation (Psorcon®), are applied 1–3 times daily. Occlusive dressings may be used for severe or resistant dermatoses. Although the manufacturer of Psorcon® states that occlusive dressings also may be used with this enhanced-potency preparation, some clinicians recommend that occlusion generally be avoided with this preparation until additional safety data are available.

Chemistry and Stability

■ Chemistry

Diflorasone diacetate is a synthetic fluorinated corticosteroid. The drug occurs as a white to buff-colored powder and is insoluble in water.

■ Stability

Diflorasone diacetate preparations should be stored in well-closed containers at 15–30°C.

For further information on chemistry, pharmacology, absorption, uses, cautions, methods of application, and use of occlusive dressings in therapy with diflorasone diacetate, see the Topical Corticosteroids General Statement 84:06.

Preparations

Diflorasone Diacetate

Topical		
Cream	0.05%	Diflorasone Diacetate Cream, Fougera, Taro
		Florone® (with propylene glycol), Dermik
		Florone E® Emollient Cream (with propylene glycol; in a hydrophilic cream base), Dermik
		Maxiflor® (with propylene glycol), Allergan
		Psorcon® (with propylene glycol), Dermik
		Psorcon E® Emollient Cream (with propylene glycol; in a hydrophilic cream base), Dermik
Ointment	0.05%	Diflorasone Diacetate Ointment, Fougera, Taro
		Florone®, Dermik
		Maxiflor®, Allergan
		Psorcon® (with propylene glycol), Dermik

Fluocinolone Acetonide
Fluocinonide

■ Fluocinolone acetonide and fluocinonide are synthetic fluorinated corticosteroids.

Uses

Fluocinolone acetonide and fluocinonide share the actions of the other topical corticosteroids and are used for the relief of the inflammatory manifestations of corticosteroid-responsive dermatoses.

Dosage and Administration

Fluocinolone acetonide shampoo should be prepared by a pharmacist at the time of dispensing the shampoo; contents of the 12-mg capsule should be mixed with the shampoo base supplied by the manufacturer. The extemporaneously prepared shampoo is stable for 3 months from the time of compounding. The extemporaneously prepared shampoo must be shaken well prior to administration.

Topical preparations of fluocinolone acetonide are applied 2–4 times daily. Fluocinonide preparations are applied topically 3 or 4 times daily. Preparations of the drugs are applied sparingly in thin films and are rubbed gently into the affected area. Occlusive dressings may be used for severe or resistant dermatoses.

Chemistry and Stability

Chemistry

Fluocinolone acetonide and fluocinonide are synthetic fluorinated corticosteroids. Fluocinolone acetonide occurs as an anhydrous or dihydrate, white or practically white, crystalline powder and is insoluble in water, soluble in alcohol, and sparingly soluble in propylene glycol. Fluocinonide, the 21-acetate ester of fluocinolone acetonide, occurs as a white to cream-colored, crystalline powder having not more than a slight odor and is practically insoluble in water and slightly soluble in alcohol.

Stability

Fluocinolone acetonide and fluocinonide preparations should be stored in tight containers at a temperature less than 40°C, preferably between 15–30°C; freezing should be avoided.

The extemporaneously prepared shampoo is stable for 3 months from time of compounding. (See Dosage and Administration.)

For further information on chemistry, pharmacology, absorption, uses, cautions, methods of application, and use of occlusive dressings in therapy with fluocinolone acetonide and fluocinonide, see the Topical Corticosteroids General Statement 84:06.

Preparations

Fluocinolone Acetonide

Topical

Cream	0.01%*	Synalar® (with parabens and propylene glycol), Medicis
	0.025%*	Synemol® Emollient Cream, Medicis
For shampoo	0.01%	Capex® Shampoo, Galderma
		FS® Shampoo (available as fluocinolone acetonide 12 mg capsule and shampoo base with parabens and propylene glycol to prepare 180 mL of shampoo), Hill
Oil	0.01%	Derma-Smoothe/FS® (with isopropyl alcohol), Hill
Ointment	0.025%*	Fluocinolone Acetonide Ointment, Fougera, G&W, Major, Moore, Zenith Goldline
		Synalar®, Medicis
Solution	0.01%*	Fluonid® (with propylene glycol), Allergan
		Synalar® (with propylene glycol), Medicis

*available by nonproprietary name

Fluocinonide

Topical

Cream	0.05%*	Fluocinonide E Emollient Cream, Alphamed, Major, Taro, Teva, Zenith Goldline
		Lidex® (with propylene glycol), Medicis
		Lidex®-E Emollient Cream (with propylene glycol), Medicis
Gel	0.05%*	Fluocinonide Gel, Fougera, Taro, Teva
		Lidex® Gel (with propylene glycol), Medicis
Ointment	0.05%*	Lidex® (with propylene glycol), Medicis
Solution	0.05%*	Lidex® (with alcohol 35% and propylene glycol), Medicis

*available by nonproprietary name

Flurandrenolide

Fluradrenolone Acetonide

Flurandrenolide is a synthetic fluorinated corticosteroid.

Uses

Flurandrenolide shares the actions of the other topical corticosteroids and is used for the relief of the inflammatory manifestations of corticosteroid-responsive dermatoses.

Dosage and Administration

Topical preparations of flurandrenolide are applied sparingly in thin films and are rubbed gently into the affected area 2 or 3 times daily. Occlusive dressings may be used for severe or resistant dermatoses. The topical dressing (tape) is generally applied as an occlusive dressing to clean, dry affected areas every 12 hours.

Chemistry and Stability

Chemistry

Flurandrenolide is a synthetic fluorinated corticosteroid. The drug occurs as a white to off-white, fluffy, crystalline powder and is practically insoluble in water and sparingly soluble in alcohol.

Stability

Flurandrenolide cream, lotion, and ointment should be protected from light and stored in tight containers at a temperature less than 40°C, preferably between 15–30°C; freezing should be avoided. Flurandrenolide tape should be stored at 15–30°C.

For further information on chemistry, pharmacology, absorption, uses, cautions, methods of application, and use of occlusive dressings in therapy with flurandrenolide, see the Topical Corticosteroids General Statement 84:06.

Preparations

Flurandrenolide

Topical

Cream	0.025%	Cordran® SP (with propylene glycol), Ocluseal
	0.05%	Cordran® SP (with propylene glycol), Ocluseal
Dressing	4 µg/cm²	Cordran® Tape, Ocluseal
Lotion	0.05%	Cordran® (with benzyl alcohol), Ocluseal
Ointment	0.025%	Cordran®, Ocluseal
	0.05	Cordran®, Ocluseal

Halcinonide

Halcinonide is a synthetic fluorinated corticosteroid.

Uses

Halcinonide shares the actions of the other topical corticosteroids and is used for the relief of the inflammatory manifestations of corticosteroid-responsive dermatoses.

Dosage and Administration

Topical preparations of halcinonide are applied sparingly in thin films and are rubbed gently into the affected area 2 or 3 times daily. Occlusive dressings may be used for severe or resistant dermatoses.

Chemistry and Stability

Chemistry

Halcinonide, a synthetic fluorinated corticosteroid, occurs as a white, crystalline powder and is insoluble in water and slightly soluble in alcohol.

Stability

Halog®-E 0.1% cream should be stored in well-closed containers at room temperature; freezing or refrigeration should be avoided. Halog® creams and

the scalp and hairy areas of the trunk and extremities, is applied and rubbed thoroughly into the affected area twice daily. Following application of the lotion, the affected area should be protected (i.e., from washing, clothing, or rubbing) until the lotion has dried. Occlusive dressings may be used for severe or resistant dermatoses.

Chemistry and Stability

■ **Chemistry**

Amcinonide is a synthetic fluorinated corticosteroid. Amcinonide occurs as a white solid and is insoluble in water.

■ **Stability**

Amcinonide cream should be stored in well-closed containers at a temperature less than 40°C, preferably between 15–30°C; freezing should be avoided. Amcinonide lotion and ointment should be stored at 15–30°C; freezing of the lotion should be avoided.

For further information on chemistry, pharmacology, absorption, uses, cautions, methods of application, and use of occlusive dressings in therapy with amcinonide, see the Topical Corticosteroids General Statement 84:06.

Preparations

Amcinonide

Topical		
Cream	0.1%	Cyclocort® (with benzyl alcohol 2% and Aquania® hydrophilic base), Fujisawa
Lotion	0.1%	Cyclocort® (with benzyl alcohol 1% w/w and Aquania® hydrophilic base), Fujisawa
Ointment	0.1%	Cyclocort® (with benzyl alcohol and propylene glycol), Fujisawa

Betamethasone

Flubenisolone

■ Betamethasone is a synthetic fluorinated corticosteroid.

Uses

Betamethasone shares the actions of the other topical corticosteroids and is used for the relief of the inflammatory manifestations of corticosteroid-responsive dermatoses.

For systemic uses of betamethasone, see 68:04.

Dosage and Administration

Betamethasone dipropionate and valerate are applied topically; concentrations of the dipropionate and valerate preparations usually are expressed in terms of betamethasone. Concentration of betamethasone valerate foam is expressed in terms of betamethasone valerate. Topical preparations of the drugs usually are applied sparingly in thin films and are rubbed gently into the affected area 1–4 times daily; betamethasone dipropionate lotions, creams, and ointments are applied once or twice daily. Dosage of 0.05% gels or lotions in an optimized (augmented) vehicle (e.g., Diprolene® AF cream, Diprolene® lotion) should not exceed 50 g or 50 mL per week, respectively; duration of therapy with these preparations should not exceed 14 days. Dosage of 0.05% ointments or creams in an optimized (augmented) vehicle should not exceed 45 g per week. When betamethasone aerosols are applied, an area about the size of the patient's hand is sprayed for not more than 3 seconds from a distance of about 15 cm 3 or 4 times daily. Betamethasone *dipropionate* preparations and betamethasone *valerate* foam preparations should *not* be used with occlusive dressings and patients should be warned that treated areas of the skin should not be bandaged or otherwise covered or wrapped as to be occlusive, unless directed by a clinician. For application to the scalp, the can containing betamethasone valerate foam should be inverted and small amounts of the preparation placed on a saucer or other cool surface. The foam should not be dispensed directly to the hands since the foam will begin to melt immediately upon contact with warm skin. Small amounts of the preparation should be massaged gently into the scalp until the foam disappears and entire scalp area has been treated.

Cautions

Betamethasone shares the toxic potentials of other topical corticosteroids, and the usual precautions of corticosteroid therapy should be observed. (See Cautions in the Topical Corticosteroids General Statement 84:06.)

Betamethasone dipropionate gels, lotions, creams, and ointments, particularly those in optimized (augmented) vehicles, are some of the most potent topical corticosteroid preparations currently available. Because of their potency, these preparations can suppress the hypothalamic-pituitary-adrenal (HPA) axis following topical application, and reversible HPA-axis suppression has occurred following topical dosages as low as 7 g, 7 mL, or 7 g of the 0.05% betamethasone dipropionate gel, lotion, or cream, respectively, in optimized (augmented) vehicles (3.5 mg of betamethasone) daily. Reversible HPA-axis suppression has also occurred following repeated topical dosages of 14 g of the 0.05% ointment in an optimized (augmented) vehicle (7 mg of betamethasone) daily in patients with psoriasis, and minimal suppression has occurred following 3.5 g of this ointment (1.75 mg of betamethasone) twice daily for 2–3 weeks in healthy individuals and in patients with psoriasis or eczema.

■ **Pediatric Precautions**

Lotrisone® cream is not recommended for use in the treatment of diaper dermatitis. Use of Diprolene® cream or ointment preparations in children younger than 12 years of age is not recommended, and the safety and efficacy of Diprolene® lotion in children younger than 12 years of age have not been established. In addition, the safety and efficacy of Luxiq® foam in pediatric patients have not been established. (See Cautions: Pediatric Precautions, in the Topical Corticosteroids General Statement 84:06.)

Chemistry and Stability

■ **Chemistry**

Betamethasone is a synthetic fluorinated corticosteroid. Betamethasone occurs as a white to practically white, crystalline powder and is miscible in water and sparingly soluble in alcohol. Betamethasone currently is commercially available for topical use only as its dipropionate and valerate esters. Betamethasone dipropionate occurs as a white to cream-white powder and is insoluble in water. Betamethasone valerate occurs as a white to practically white powder and is practically insoluble in water and soluble in alcohol.

■ **Stability**

Betamethasone preparations should be stored as directed by the manufacturer.

For further information on chemistry, pharmacology, absorption, uses, cautions, methods of application, and use of occlusive dressings in therapy with betamethasone, see the Topical Corticosteroids General Statement 84:06.

Preparations

Betamethasone Dipropionate

Topical		
Aerosol	60 µg (of betamethasone) per 3-second spray	Diprosone® Aerosol (with isopropyl alcohol 10% and hydrocarbon propellants), Schering
Cream	0.05% (of betamethasone)*	Alphatrex®, Savage
		Del-Beta®, Del-Ray
		Diprolene® AF (with propylene glycol in an optimized [augmented] vehicle), Schering
		Diprosone® (with propylene glycol), Schering
		Maxivate®, Westwood-Squibb
Gel	0.05% (of betamethasone)	Diprolene® (with propylene glycol in an optimized [augmented] vehicle), Schering
Lotion	0.05% (of betamethasone)*	Alphatrex® (with isopropyl alcohol), Savage
		Del-Beta®, Del-Ray
		Diprolene® Lotion (with isopropyl alcohol 30% and propylene glycol in an optimized [augmented] vehicle), Schering
		Diprosone® (with isostearyl alcohol 46.8%), Schering
		Maxivate® (with isopropyl alcohol), Westwood-Squibb
Ointment	0.05% (of betamethasone)*	Alphatrex®, Savage
		Betamethasone Dipropionate Augmented Ointment, Alphamma, Warrick
		Diprolene® (with propylene glycol in an optimized [augmented] vehicle), Schering

Acinetobacter, Citrobacter, Enterobacter, Providencia, Serratia, and streptococci in vitro. *Candida albicans* may be inhibited by silver sulfadiazine concentrations of 50–100 μg/mL, and *Herpesvirus hominis* may be inhibited by 10 μg/mL. In higher concentrations, the drug inhibits *Clostridium perfringens.*

Pharmacokinetics

Silver sulfadiazine itself does not appear to be absorbed. When in contact with body tissues and fluids, silver sulfadiazine slowly reacts with sodium chloride, sulfhydryl groups, and protein, resulting in the release of sulfadiazine. Sulfadiazine may be systemically absorbed from the site of application, particularly when silver sulfadiazine is applied to second-degree burns. When the drug is applied to extensive burns, serum sulfadiazine concentrations of up to 12 mg/dL have been reported. In one study, patients who were treated with 5–10 g of silver sulfadiazine daily applied as a 1% cream were found to have blood sulfadiazine concentrations of 1–2 mg/dL; 100–200 mg of sulfadiazine was excreted in urine within 24 hours following application of the cream. When 5–15 g/kg of a cream containing 1% silver sulfadiazine was applied daily for 100 days to experimentally abraded areas on rabbits, an unidentified silver compound was deposited in renal tissue; however, concurrent impairment of renal function was not noted.

Chemistry and Stability

Chemistry

Silver sulfadiazine is a synthetic anti-infective agent produced by the reaction of silver nitrate with sulfadiazine. Silver sulfadiazine occurs as a white, fluffy powder and is practically insoluble in water. The commercially available cream contains silver sulfadiazine in micronized form.

Stability

Silver sulfadiazine cream should be stored at 15–30°C.

Silver sulfadiazine reacts with most heavy metals; this reaction may result in release of free silver and darkening of the cream. If this occurs, the cream should be discarded. When silver sulfadiazine is used in conjunction with topical proteolytic enzymes, the possibility that silver may inactivate the proteolytic enzymes should be considered; however, the manufacturer of Silvadene (no longer commercially available in the US) has stated that this did not occur with its product.

Preparations

Silver Sulfadiazine

Topical

Cream	1%*	SSD® (with cetyl alcohol, methylparaben, and propylene glycol), Par
		SSD AF® (with methylparaben and propylene glycol), Par
		Silvadene® (with methylparaben and propylene glycol), Monarch
		Thermazene® (with methylparaben and propylene glycol), Major, Par, Sherwood, Zenith Goldline

*available by nonproprietary name

ANTI-INFLAMMATORY AGENTS 84:06

Topical Corticosteroids General Statement

Hydrocortisone or synthetic derivatives of hydrocortisone are used topically as anti-inflammatory agents.

Uses

Dermatoses

Topical corticosteroids are used for the symptomatic relief of inflammatory dermatoses. The cause of the dermatoses should be determined and eliminated if possible; dermatoses are controlled but not cured by these drugs. Although systemic corticosteroids are more effective in most dermatologic inflammations, topical treatment is preferred in most responsive cases because it causes fewer adverse systemic effects.

Topical corticosteroids generally are most effective in the treatment of acute or chronic dermatoses such as seborrheic or atopic dermatitis, localized neurodermatitis, anogenital pruritus, psoriasis (particularly of the face and between skin folds), and the inflammatory phase of xerosis. Topical corticosteroids are effective in the late phase of allergic contact dermatitis or irritant dermatitis, but systemic corticosteroids are usually required to relieve the acute manifestations of these dermatoses.

Individual topical corticosteroid preparations vary in anti-inflammatory activity (as measured by vasoconstrictor assay) and in percutaneous penetration, but therapeutic efficacy of a particular drug can often be increased by increasing the concentration or by using occlusive dressing therapy. As with systemic use, some patients may respond better to one topical corticosteroid than to another. Topical corticosteroid preparations may be grouped according to relative anti-inflammatory activity, but *activity may vary considerably depending upon the vehicle, the site of application, disease, the individual patient, and whether or not an occlusive dressing is used.* (See Pharmacokinetics.) *Approximate* relative activity (based principally on vasoconstrictor assay and/or clinical effectiveness in psoriasis) of some topical corticosteroid preparations in decreasing order is as follows (preparations in each group are approximately equivalent):

Group I

Betamethasone dipropionate (Diprosone®) cream (optimized vehicle) or ointment (optimized vehicle) 0.05% (of betamethasone)
Betamethasone dipropionate (Diprolene® AF) cream 0.05% (of betamethasone)
Clobetasol propionate (Temovate®, Olux®) cream, foam, or ointment 0.05%
Diflorasone diacetate (Psorcon®) ointment (optimized vehicle) 0.05%

Group II

Amcinonide (Cyclocort®) ointment 0.1%
Betamethasone dipropionate (Diprosone®) ointment 0.05% (of betamethasone)
Desoximetasone (Topicort®) cream or ointment 0.25%
Desoximetasone (Topicort®) gel 0.05%
Diflorasone diacetate (Florone®, Maxiflor®) ointment 0.05%
Fluocinonide (Lidex®) cream or ointment 0.05%
Fluocinonide gel 0.05%
Halcinonide (Halog®) cream 0.1%

Group III

Betamethasone benzoate gel 0.025%
Betamethasone dipropionate (Diprosone®) cream 0.05% (of betamethasone)
Betamethasone valerate (Valisone®) ointment 0.1% (of betamethasone)
Diflorasone diacetate (Florone®, Maxiflor®) cream 0.05%
Mometasone furoate (Elocon®) ointment 0.1%
Triamcinolone acetonide (Aristocort®) cream 0.5%

Group IV

Desoximetasone (Topicort® LP) cream 0.05%
Fluocinolone acetonide (Synalar-HP®) cream 0.2%
Fluocinolone acetonide (Synalar®) ointment 0.025%
Flurandrenolide (Cordran®) ointment 0.05%
Triamcinolone acetonide (Aristocort®, Kenalog®) ointment 0.1%

Group V

Betamethasone benzoate cream 0.025%
Betamethasone dipropionate (Diprosone®) lotion 0.05% (of betamethasone)
Betamethasone valerate (Valisone®) cream 0.1% (of betamethasone)
Betamethasone valerate (Valisone®) lotion 0.1% (of betamethasone)
Fluocinolone acetonide (Synalar®) cream 0.025%
Flurandrenolide (Cordran®) cream 0.05%
Hydrocortisone butyrate (Locoid®) cream 0.1%
Hydrocortisone valerate (Westcort®) cream 0.2%
Prednicarbate (Dermatop® Emollient) cream 0.1%
Triamcinolone acetonide (Kenalog®) cream 0.1%
Triamcinolone acetonide (Kenalog®) lotion 0.1%

Group VI

Alclometasone dipropionate (Aclovate®) cream or ointment 0.05%
Desonide (Tridesilon®) cream 0.05%
Fluocinolone acetonide (Synalar®) solution 0.01%